

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
30 September 2004 (30.09.2004)

PCT

(10) International Publication Number
WO 2004/082722 A3

- (51) International Patent Classification⁷: **A61K 49/08**, 51/06
- (21) International Application Number: PCT/EP2004/050329
- (22) International Filing Date: 18 March 2004 (18.03.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
03006061.0 19 March 2003 (19.03.2003) EP
- (71) Applicants (for all designated States except US): **Kantonsspital Basel** [CH/CH]; Hebelstrasse 30, CH-4031 Basel (CH). **Universität Bern** [CH/CH]; Hochschulstrasse 4, CH-3012 Bern (CH).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **MERLO, Adrian** [CH/CH]; Im Stigler 8, CH-4312 Magden (CH). **MÄCKE, Helmut** [DE/DE]; Bergfriedweg 7, 79539 Lörrach (DE). **REUBI, Jean-Claude** [CH/CH]; Austrasse 4, CH-3084 Wabern (CH). **GOOD, Stephan** [CH/CH]; Steinrebenstrasse 108, CH-4153 Reinach (CH).
- (74) Agent: **MAUÉ, Paul Georg**; Solvias AG, Patents WKL-402.3.04, Klybeckstr. 191, CH-4002 Basel (CH).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
- with international search report
 - before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report:
6 January 2005
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: RADIOLABELED CONJUGATES BASED ON SUBSTANCE P AND THE USES THEREOF

(57) Abstract: Radionuclide labelled conjugates based on substance P and analogues thereof with the chelator (DOTAGA) (1-(1-(3-carboxy-3-carboxy-propyl)-4,7, 10(carboxymethyl)-1,4,7,10-tetraazacyclo-dodecane, DOTASA (1-(1-(3-carboxy-2carboxy-ethyl)-4,7, 10 (carboxymethyl)-1,4,7, 10-tetraazacyclo-dodecane, or chelator (DOTA) [1,4,7, 10 tetraazaacyclo-dodecane-1,4,7, 1 0-tetra(acetic acid)] are useful radiopharmaceutical substances for targeting and treatment of brain tumors, especially gliomas.

WO 2004/082722 A3

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/050329

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K49/08 A61K51/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/24235 A (POWELL PIA ;EISENWIENER KLAUS (DE); MAECKE HELMUT R (DE); MALLINCK) 28 March 2002 (2002-03-28) page 3, lines 1-29; claims 2,11-14 example 7; table 3	1,2, 10-15
X	WO 01/02021 A (ORTIZ ARMUA PEDRO) 11 January 2001 (2001-01-11) claims 5-9,14,20-22	1,2, 10-16
P,X	FICHNA J. ET AL: "Synthesis of target specific radiolabeled peptides for diagnostic imaging" BIOCONJUGATE CHEM, vol. 14, 2003, pages 3-17, XP001172817 page 11, paragraph 7; figures 1,8; tables 4,5	1,2, 10-15
	-/--	

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the international search

29 October 2004

Date of mailing of the international search report

05/11/2004

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2260 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Gonzalez Ramon, N

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP2004/050329

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	NIKULA, T. K. ET AL: "Improved method for labelling DOTA-analogues with ²¹³ Bi, ²²⁵ Ac and lanthanides" ABSTRACTS OF PAPERS 225 ACS NATIONAL MEETING, 23 March 2003 (2003-03-23), - 27 March 2003 (2003-03-27) page Nucl-067, XP008023978 abstract	1,2, 13-15
A	LAZNICEK M ET AL: "Octreotide and octreotate derivatives radiolabeled with yttrium: Pharmacokinetics in rats." CANCER BIOTHERAPY AND RADIOPHARMACEUTICALS, vol. 17, no. 5, 2002, pages 527-533, XP008023912 ISSN: 1084-9785 page 533, column 1, paragraph 2; figure 1	1-16
A	EP 1 283 216 A (MALLINCKRODT INC) 12 February 2003 (2003-02-12) example 3	1-16
A	HEPPELER A ET AL: "RECEPTOR TARGETING FOR TUMOR LOCALISATION AND THERAPY WITH RADIOPEPTIDES" CURRENT MEDICINAL CHEMISTRY, BENTHAM SCIENCE PUBLISHERS BV, BE, vol. 7, no. 9, 2000, pages 971-994, XP000982225 ISSN: 0929-8673 page 986, column 1; table 1	1-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2004/050329

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-13 are directed to a method of treatment of the human/animal body/ diagnostic method practised on the human/animal body, Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/050329

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 0224235	A	28-03-2002	AT 271396 T	15-08-2004
			AU 7748801 A	02-04-2002
			DE 60104421 D1	26-08-2004
			WO 0224235 A2	28-03-2002
			EP 1289571 A2	12-03-2003
			JP 2004509152 T	25-03-2004
WO 0102021	A	11-01-2001	AU 6718900 A	22-01-2001
			EP 1196200 A2	17-04-2002
			WO 0102021 A2	11-01-2001
			ZA 200200096 A	04-04-2003
EP 1283216	A	12-02-2003	EP 1283216 A1	12-02-2003
			CA 2456881 A1	20-02-2003
			WO 03014158 A1	20-02-2003
			EP 1419178 A1	19-05-2004